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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/785,374	02/24/2004	Marshall L. Summar	1242/58	1629

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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	**PAPER NUMBER**
1634	

MAIL DATE	DELIVERY MODE
09/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/785,374	SUMMAR ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *11-17,24 and 30-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,18-23,25-29 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0804;0905;0306;0906;0407*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, and of the species of cardiac surgery, pulmonary hypertension, and citrulline, in the reply filed on March 26, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's corrected identification of claims readable on the elected species filed July 2, 2007 is also acknowledged. However, it is noted that applicant has included the claims of non-elected Group II (claims 30-33) among those readable on the elected species. Because those claims are drawn to a non-elected invention, they are withdrawn from consideration (see below). Accordingly, the following claims reading on the elected invention have been examined: claims 1-10, 18-23, 25-29 and 34.

2. Claims 11-17, 24, and 30-33, as well as species other than the elected species noted above, are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on March 26, 2007.

Priority

3. It is noted that the elected inventions encompassed by claims 1 and 18 and claims dependent therefrom (specifically, the environmental stimulus of cardiac surgery and the disorder of pulmonary hypertension) were first disclosed in parent application 09/585,077; accordingly, the effective filing date applicable to those claims is that of the

'077 application, specifically, June 1, 2000. As the method of claim 25 and claims dependent therefrom (drawn to "raising a level of a nitric acid precursor") was first disclosed in the present application, the effective filing date applicable to those claims is that of the instant application, specifically, February 24, 2004.

4. It is also noted that as application 09/585,077 has been patented, the specification should be amended so as to provide the current status of the '077 application.

Information Disclosure Statement

5. The information disclosure statement filed August 19, 2004 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The following references were not considered because copies were not provided: numbers 25 (Boger et al), 29 (Maxwell et al), 32 (Maxwell et al), 38 (Vosatka), and 46 (Alves et al). With regard to the same IDS, it is noted that the following references are located in application file 09/585,077: numbers 48-50, 52-57 and 59; and that the following references are located in application file 09/323,472: 51, 58, and 60-61.

Specification

6. The specification fails to comply with one or more of the requirements of 37 CFR § 1.821 through 1.825 because the specification recites sequences that lack description by the appropriate sequence identifier set forth in the "Sequence Listing" as required by

37 CFR § 1.821(d). See, for example, page 66. Appropriate corrections for compliance are required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 18-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18-23 are indefinite because it is not clear whether the claims are drawn to methods of "treating or preventing" a disorder as set forth in the preamble of claim 18, or to methods that merely require administering a "therapeutically effective amount of a nitric oxide precursor" to any "subject in need thereof," as set forth in the method step of the claim. It is not clear how the method step performed during the practice of the claimed invention actually relates to or results in the particular treatment or prevention set forth in the preamble. Clarification is required.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-4, 6-10, 18-23, and 25-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Waugh (US 5,874,471A [23 February 1999]).

Waugh discloses methods in which citrulline is administered to a subject to achieve various therapeutic and/or prophylactic effects (see entire reference). It is noted that Waugh teaches that their methods function by increasing the availability of substrate for nitric oxide production (see, e.g., col 10, line 61-col 11, line 17).

Waugh discloses the administration of citrulline to humans "in dosage range from about 1.7 to about 20 grams per day" to achieve "beneficial therapeutic effects" for a variety of conditions (see col 11, lines 18-27). Waugh further discloses the oral administration of capsules containing approximately 876 mg of citrulline (see, e.g., col 17, lines 1-6). Thus, Waugh discloses administration of a dose of citrulline meeting the requirements of, e.g., dependent claims 8-9, 21-22, and 28-29, and within the range disclosed in the specification at page 51.

With further regard to dependent claim 3, it is noted that the language of the claim does not result in any manipulative difference between the claimed invention and the method of Waugh; as Waugh disclose administration of citrulline in a manner meeting the requirements of the claim, Waugh also inherently anticipates the methods of claim 3. Regarding the inventions of claims 4 and 6, it is noted that Waugh's teaching of the prevention of "angiostenosis after angioplasty" (see col 11, lines 18-27) constitutes a type of "cardiac surgery" meeting the requirements of claim 6. With regard to claim 18 and claims dependent therefrom, which recite the elected species of "pulmonary hypertension," the claims as written merely require the administration of

citrulline in a "therapeutically effective" amount, and (as discussed above) Waugh clearly teaches the administration of citrulline in dosages encompassed by the claims, such that Waugh inherently anticipates the claimed invention. There is no manipulative difference between the method of Waugh and that of the claims. With further regard to the preamble of claim 18, reciting "treating or preventing....pulmonary hypertension," it is also noted that MPEP 2111.02 states:

> If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction. *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir.1999).

In the instant case, the preamble of the claim merely recites the intended use of the invention, and Waugh's disclosure of a method step meeting the requirements of the claim anticipates the claimed invention.

With further regard to claim 25 and claims dependent therefrom, it is again noted that Waugh discloses that his method functions by increasing the availability of substrate for nitric oxide production (see, e.g., col 10, line 61-col 11, line 17); thus, the method disclosed by Waugh also achieves the objective of "raising a level of a nitric oxide precursor."

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 5 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waugh (US 5,874,471A [23 February 1999]) in view of Kaesemeyer (US 5,767,160A [16 June 1998]).

Waugh discloses methods in which citrulline is administered to a subject to achieve various therapeutic and/or prophylactic effects (see entire reference). It is noted that Waugh teaches that their methods function by increasing the availability of substrate for nitric oxide production (see, e.g., col 10, line 61-col 11, line 17).

Waugh discloses the administration of citrulline to humans "in dosage range from about 1.7 to about 20 grams per day" to achieve "beneficial therapeutic effects" for a variety of conditions (see col 11, lines 18-27). Waugh further discloses the oral administration of capsules containing approximately 876 mg of citrulline (see, e.g., col 17, lines 1-6). Thus, Waugh discloses administration of a dose of citrulline within the ranges disclosed in the specification at page 51.

While Waugh discloses the administration of citrulline for "vasoprotection" (see, e.g., col 12, lines 20-31) and in the prevention or treatment of "vasospastic diseases," preeclampsia and the "prevention of angiostenosis after angioplasty" (see, e.g., col 11, lines 18-27), Waugh does not disclose the administration of citrulline therapy to a subject suffering from pulmonary hypertension (as set forth in claim 5) or a subject exposed to or about to be exposed to the environmental stimulus of "increased postoperative pulmonary vascular tone associated with cardiac surgery" (as set forth in claim 34).

Kaesemeyer teaches the use of arginine and its "biological equivalent" citrulline in the treatment of pulmonary hypertension as well as "perioperative hypertension" and "control of blood pressure in the treatment of hypertensive crisis," as well as in the treatment and prevention of various complications of heart surgery (see entire reference, particularly col 4 lines 36-60 and col 6, lines 5-45).

In view of the teachings of Kaesemeyer, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have administered citrulline in the manner disclosed by Waugh to a subject suffering from pulmonary hypertension or to a subject exposed to or about to be exposed to the environmental stimulus of "increased postoperative pulmonary vascular tone associated with cardiac surgery." As Kaesemeyer suggests the use of citrulline in the treatment of pulmonary hypertension as well as in a wide variety of other types of hypertension and for the treatment of cardiac surgery complications, an ordinary artisan would have been motivated to have administered citrulline as described by Waugh to subjects suffering

from these conditions for the advantage of alleviating hypertension and reducing pulmonary vascular tone following cardiac surgery, as suggested by the teachings of Kaesemeyer.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-10, 18-23, 25-29 and 34 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,743,823 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

The claims of the '823 patent recite steps of administering citrulline in dosages encompassed by the instant claims to subjects suffering from the same conditions recited in the instant claims and elected by applicant (specifically, cardiac surgery,

pulmonary hypertension). The instant claims differ from the '823 claims in that the instant claims do not require the polymorphism detection steps set forth in the '823 claims. However, the instant claims, in simply lacking a step of the '823 claims, encompass the methods set forth the '823 claims, and are anticipated by those claims. With further regard to instant claims 25-29, it is noted that the method steps of the '823 claims comprise administering citrulline as in the instant claims, and therefore inherently achieve the same result of "raising a level of a nitric oxide precursor;" the mere recitation of this inherent result in the instant claims does not result in a manipulative difference between the claimed inventions nor render them patentably distinct. With further regard to claim 34, it is noted that the '823 specification defines the environmental stimulus of "cardiac surgery" as encompassing "increased postoperative pulmonary vascular tone;" accordingly, claim 34 is inherently anticipated by the '823 claims. Thus, the instant claims and the '823 claims are not patentably distinct.

Conclusion

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday and Thursday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571/272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Diana B. Johannsen
Primary Examiner
Art Unit 1634